

Notice of Allowability	Application No.	Applicant(s)	
	10/057,783	FORSTER ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 3/22/05.
2. ☒ The allowed claim(s) is/are 1,2,4-11,13-17,19,23-42,44 and 52-54.
3. ☒ The drawings filed on 25 January 2002 are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|--|
| <ol style="list-style-type: none"> 1. <input type="checkbox"/> Notice of References Cited (PTO-892) 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____ 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | <ol style="list-style-type: none"> 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>4/14/05;5/20/05</u>. 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance 9. <input type="checkbox"/> Other _____ |
|---|--|

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An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ignacio Perez de la Cruz on May 20, 2005.

Examiner's Amendments to the Claims:

Cancel claim 55.

Claim 1, 7-10, 32, 33 and 42 have been amended as follows:

1. (Currently Amended) A reconstituted cell-free translation system, which lacks more than one active wild-type elongator amino acyl tRNA species, for generating a peptidomimetic product comprising:

(a) purified translation factors; and

(b) more than one elongator tRNA species which (i) is charged with a non-naturally occurring amino acid or amino acid analog, and (ii) recognizes a trinucleotide sense codon,

wherein the elongator tRNA species charged with a non-naturally occurring amino acid or amino acid analog replaces the wild-type elongator amino acyl tRNA species,

wherein the cell-free translation system translates exogenously added mRNA species with highly selective incorporation at each of said trinucleotide sense codons to form the peptidomimetic product,

wherein the peptidomimetic product comprises said non-naturally occurring amino acids or amino acid analogs, and

wherein the system lacks the ability to synthesize ~~at least one~~ the wild-type amino

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acyl tRNA species.

7. (Currently Amended) A cell-free translation system comprising purified translation factors and tRNA species that translates exogenously added mRNA species to form a peptidomimetic product, which system

- (a) lacks more than one active wild-type elongator amino acyl tRNA species and lacks the ability to synthesize said wild-type amino acyl tRNA species, and
- (b) comprises more than one exogenous elongator amino acyl tRNA species charged with a non-natural amino acid species or amino acid analog, the exogenous elongator amino acyl tRNA species replacing said wild-type elongator amino acyl tRNA species.

8. (Currently Amended) A cell-free translation system comprising purified translation factors and tRNA species that translates exogenously added mRNAs to form a peptidomimetic product, which system

- (a) lacks one or more active wild-type amino acyl tRNA species and lacks the ability to synthesize said wild-type amino acyl tRNA species,
- (b) ~~includes~~ comprises at least one exogenous amino acyl tRNA species charged with a non-natural amino acid species or amino acid analog, the exogenous amino acyl tRNA species replacing said active wild-type amino acyl tRNA species, and
- (c) comprises a plurality of different mRNA species encoding a plurality of peptidomimetic products.

9. (Currently Amended) A kit for translating exogenously added mRNA to form a peptidomimetic product, the kit comprising:

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- (a) a reconstituted cell-free translation system that lacks more than one active wild-type elongator amino acyl tRNA species, comprising: purified translation factors and more than one elongator tRNA species charged with a non-naturally occurring amino acid or amino acid analog ~~capable of translating~~ that translates exogenously added mRNA species with highly selective incorporation at each codon to form a peptidomimetic product, wherein the elongator tRNA species charged with a non-naturally occurring amino acid or amino acid analog replaces the wild-type elongator amino acyl tRNA species, and wherein the system lacks the ability to synthesize the wild-type amino acyl tRNA species; and
- (b) instructions associated ~~there with~~ therewith for using the kit for translating exogenously added mRNA to form a peptidomimetic product.
10. (Currently Amended) A kit for translating exogenously added mRNA to form a peptidomimetic product, the kit comprising:
- (a) a cell-free translation system comprising purified translation factors and tRNA species ~~capable of translating that translates~~ exogenously added mRNA species to form a peptidomimetic product, which system
- (i) lacks more than one active wild-type elongator amino acyl tRNA species and lacks the ability to synthesize said wild-type amino acyl tRNA species,
- (ii) ~~includes~~ comprises more than one exogenous elongator amino acyl tRNA species charged with a non-natural amino acid species or amino acid analog, the exogenous elongator amino acid acyl tRNA species replacing said wild-type elongator amino acyl tRNA species; and

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- (b) ~~comprises~~ instructions associated therewith for using the kit for translating exogenously added mRNA to form a peptidomimetic product.
32. (Currently Amended) The translation system of claim 1, wherein the peptidomimetic product comprises more than two ~~unnatural~~ non-naturally occurring amino acids or amino acid analogs.
33. (Currently Amended) The translation system of claim 31, wherein the peptidomimetic product comprises five ~~unnatural~~ non-naturally occurring amino acids or amino acid analogs.
42. (Currently Amended) The translation system of claim 1, wherein the peptidomimetic product comprises ~~an-unnatural~~ a non-natural backbone.

The following is an **Examiner's Statement of Reasons for Allowance**: The following reference appears to be the closest art to the claimed invention: Rothschild *et al.* (U. S. Patent 5,643,772) teach a preparation of nascent proteins translated in a cell-free translation system using non-radioactive markers (e.g., coumarin amino acid or dansyllysine), where a non-radioactive marker is misaminoacylated to a tRNA molecule, and the misaminoacylated tRNA is added to the translation system and incubated to incorporate marker into the peptide, and cell-free translation systems include *E. coli* lysates, or wheat germ extracts, and mixtures of purified translation factors or combination of lysates or lysates supplemented with purified translation factors. However, the reference does not teach or suggest a cell-free translation system comprising purified translation factors and more than one exogenous elongator amino acyl tRNA species charged with a non-natural amino acid species or amino acid analog that translates exogenously added mRNA species with highly selective incorporation at each of the trinucleotide sense codons to form a peptidomimetic product, where the exogenous elongator amino acyl tRNA species replaces the wild-type elongator amino acyl tRNA species, and the system lacks more than one active wild-type elongator amino acyl tRNA species and lacks the ability to synthesize said wild-type amino acyl tRNA species. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. *CMK*
Patent Examiner

CMK
May 20, 2005

A handwritten signature in cursive script, reading "Karen Cochrane Carlson PhD".

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

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Proposed Examiner's Amendments to the Claims:

Cancel claim 55.

Claim 1, 2, 4, 7-10, 32, 33 and 42 have been amended as follows:

1. (Currently Amended) A reconstituted cell-free translation system, which lacks more than one active wild-type elongator amino acyl tRNA species, for generating a peptidomimetic product comprising:

(a) purified translation factors; and

(b) more than one elongator tRNA species which (i) is charged with a non-naturally occurring amino acid or amino acid analog, and (ii) recognizes a trinucleotide sense codon,

wherein the elongator tRNA species charged with a non-naturally occurring amino acid or amino acid analog replaces the wild-type elongator amino acyl tRNA species,

wherein the cell-free translation system translates exogenously added mRNA species with highly selective incorporation at each of said trinucleotide sense codons to form the peptidomimetic product,

wherein the peptidomimetic product comprises said non-naturally occurring amino acids or amino acid analogs, and

wherein the system lacks the ability to synthesize ~~at least one~~ the wild-type amino acyl tRNA species.

2. (Currently Amended) The translation system of claim 1 for generating a peptidomimetic product, which system is ~~substantially~~ free of the translation factors EF-P, W, W2 and rescue.

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4. (Currently Amended) The translation system of claim 1 for generating a peptidomimetic product, which system is ~~substantially~~ free of a translation factor selected from the group consisting of EF-P, W, W2 and rescue.
7. (Currently Amended) A cell-free translation system comprising purified translation factors and tRNA species that translates exogenously added mRNA species to form a peptidomimetic product, which system
- (a) lacks more than one active wild-type elongator amino acyl tRNA species and lacks the ability to synthesize said wild-type amino acyl tRNA species, and
 - (b) comprises more than one exogenous elongator amino acyl tRNA species charged with a non-natural amino acid species or amino acid analog, the exogenous elongator amino acyl tRNA species replacing said wild-type elongator amino acyl tRNA species.
8. (Currently Amended) A cell-free translation system comprising purified translation factors and tRNA species that translates exogenously added mRNAs to form a peptidomimetic product, which system
- (a) lacks one or more active wild-type amino acyl tRNA species and lacks the ability to synthesize said wild-type amino acyl tRNA species,
 - (b) ~~includes~~ comprises at least one exogenous amino acyl tRNA species charged with a non-natural amino acid species or amino acid analog, the exogenous amino acyl tRNA species replacing said active wild-type amino acyl tRNA species, and
 - (c) comprises a plurality of different mRNA species encoding a plurality of peptidomimetic products.

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9. (Currently Amended) A kit for translating exogenously added mRNA to form a peptidomimetic product, the kit comprising:

(a) a reconstituted cell-free translation system that lacks more than one active wild-type elongator amino acyl tRNA species, comprising: purified translation factors and more than one elongator tRNA species charged with a non-naturally occurring amino acid or amino acid analog capable of translating that translates exogenously added mRNA species with highly selective incorporation at each codon to form a peptidomimetic product, wherein the elongator tRNA species charged with a non-naturally occurring amino acid or amino acid analog replaces the wild-type elongator amino acyl tRNA species, and wherein the system lacks the ability to synthesize the wild-type amino acyl tRNA species; and

(b) instructions associated ~~there with~~ therewith for using the kit for translating exogenously added mRNA to form a peptidomimetic product.

10. (Currently Amended) A kit for translating exogenously added mRNA to form a peptidomimetic product, the kit comprising:

(a) a cell-free translation system comprising purified translation factors and tRNA species ~~capable of translating that translates~~ exogenously added mRNA species to form a peptidomimetic product, which system

(i) lacks more than one active wild-type elongator amino acyl tRNA species and lacks the ability to synthesize said wild-type amino acyl tRNA species,

(ii) ~~includes~~ comprises more than one exogenous elongator amino acyl tRNA species charged with a non-natural amino acid species or amino acid analog, the exogenous

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elongator amino acid acyl tRNA species replacing said wild-type elongator amino acyl tRNA species; and

(b) ~~comprises~~ instructions associated therewith for using the kit for translating exogenously added mRNA to form a peptidomimetic product.

32. (Currently Amended) The translation system of claim 1, wherein the peptidomimetic product comprises more than two ~~unnatural~~ non-naturally occurring amino acids or amino acid analogs.

33. (Currently Amended) The translation system of claim 31, wherein the peptidomimetic product comprises five ~~unnatural~~ non-naturally occurring amino acids or amino acid analogs.

42. (Currently Amended) The translation system of claim 1, wherein the peptidomimetic product comprises ~~an-unnatural~~ a non-natural backbone.